

CLAIMS

1. A method for analysing the metabolites of a biological sample which comprises quantitatively determining one or more metabolites in said sample in a way that said quantitative determination resolves isotopic mass differences within one metabolite,
said method being characterized in that the sample comprises or is derived from a cell which has been maintained under conditions allowing the uptake of an isotopically labeled metabolizable compound so that the metabolites in said cell are saturated with the isotope with which said metabolizable compound is labeled.
2. The method of claim 1, further comprising, prior to quantitative determining the metabolites, combining the biological sample (i.e. the first biological sample) with a second biological sample in which the metabolites are not isotopically labeled or are isotopically labeled differently from the first biological sample; and determining in said biological samples the relative quantity of metabolites which differ by their isotopic label.
3. The method of claim 2, wherein the first and the second biological sample correspond to different phenotypic and/or genotypic states of the cells comprised in the samples or from which the samples are derived.
4. The method of claim 3; wherein the different phenotypic and/or genotypic states are different developmental stages, environments, nutritional supplies, taxonomic units, wild-type and mutant or transgenic genomes, infected and uninfected states, diseased and healthy states or different stages of a pathogenicity.
5. The method of any one of claims 1 to 4, wherein at least 50 metabolites are quantitatively determined.

6. The method of any one of claims 1 to 5, wherein the metabolites comprise sugars, sugar alcohols, organic acids, amino acids, fatty acids, vitamins, sterols, phosphates, polyamines, polyols, nucleosides, adenine, ethanolamine, nicotinic acid, uracil and/or urea.
7. The method of any one of claim 1 to 6, wherein the isotope is ^{13}C , ^{15}N , ^{18}O or ^2H .
8. The method of claim 7, wherein the isotopically labeled metabolizable compound is $\text{U-}^{13}\text{C}$ -glucose, $^2\text{H}_2\text{O}$, H_2^{18}O , $\text{U-}^{13}\text{C}$ acidic acid, ^{13}C carbonate or ^{13}C carbonic acid.
9. The method of any one of claims 1 to 8, wherein the biological sample comprises yeast cells or plant cells.
10. The method of any one of claims 1 to 9, further comprising fractionating or purifying the biological sample so that the sample contains a subset of the metabolites contained in the cell from which the sample is derived.
11. The method of any one of claims 1 to 10, wherein the metabolites are quantitatively determined by mass spectrometry.
12. The method of claim 11, wherein mass spectrometry is MALDI-TOF.
13. The method of any one of claims 1 to 12, wherein the metabolites are chromatographically separated prior to quantitative determination.
14. The method of any one of claims 1 to 13, further comprising the step of introducing external standards for one or more of the quantitatively determined metabolites.
15. The method of any one of claims 1 to 14, further comprising the step of identifying one or more of the metabolites which are quantitatively determined.

16. The method of claim 15, wherein said metabolites are identified by secondary fragmentation.
17. The method of claim 16, wherein identifying of said metabolites comprises electron impact ionisation, MS-MS technology and/or post source decay analyses of molecular ions or fragments.
18. The method of any one of claims 1 to 17, wherein said cell has been maintained under conditions additionally allowing the uptake of an isotopically unlabeled metabolizable compound and said compound and/or metabolic products thereof are quantitatively determined.
19. The method of claim 18, wherein the amount determined for the isotopically unlabeled metabolizable compound and/or said metabolic products thereof is compared with the amount obtained by carrying out said method correspondingly, but without the uptake of said unlabeled metabolizable compound.
20. The method of any one of claims 1 to 19, wherein, in addition to metabolites, one or more proteins and/or transcripts in said sample(s) is/are quantitatively determined and analysed.
21. The method of claim 20, wherein said metabolites and proteins and/or transcripts are each determined from the same biological sample.
22. The method of any one of claims 1 to 21, wherein said analysing further involves suitable statistical evaluation and correlation analyses of the data obtained and, optionally, network analyses.
23. A set of isotopically labeled metabolites obtainable from a sample which comprises or is derived from a cell which has been maintained under conditions allowing the uptake of an isotopically labeled metabolizable

compound so that the metabolites in said cell are saturated with the isotope with which said metabolizable compound is labeled.

24. Use of the set of isotopically labeled metabolites of claim 23 as a quantitative standard for determining the amount of one or more metabolites in a biological sample.
25. A kit comprising an isotopically labeled metabolizable compound and a manual for use in carrying in out the method of any one of claims 1 to 22 or the set of isotopically labeled metabolites of claim 23.
26. Use of an isotopically labeled compound that can be metabolized by a cell for labeling the metabolites in said cell in a saturating manner.
27. Use of an isotopically labeled compound that can be metabolized by a cell for the quantitative determination of metabolites in a biological sample comprising or being derived from said cell.
28. Use of an isotopically labeled compound that can be metabolized by a cell for analysing the metabolite profile of a biological sample comprising or being derived from said cell.